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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
01/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,760	DORING ET AL.	
	Examiner	Art Unit	
	JONATHAN S. LAU	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-67 and 70-89* is/are pending in the application.

4a) Of the above claim(s) *52-67 and 83-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-51 and 70-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 8 Oct 2009, in which claims 49, 70 and 81 are amended to change the scope and breadth of the claim; claims 74, 76, 77, 79 and 80 are amended to correct minor informalities and claims 68 and 69 are canceled.

This application is the national stage entry of PCT/EP04/06848, filed 24 Jun 2004; and claims benefit of foreign priority document EPO 03013457.1, filed 24 Jun 2003; and claims benefit of foreign priority document EPO 03027750.3, filed 02 Dec 2003; currently a certified copy of foreign priority document EPO 03013457.1, filed 24 Jun 2003, and EPO 03027750.3, filed 02 Dec 2003 has not been made of record.

Claims 49-67 and 70-89 are pending in the current application. Claims 52-67 and 83-89, drawn to non-elected inventions, are withdrawn. Claims 49-51 and 70-82 are examined on the merits herein.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications EPO 03013457.1, filed 24 Jun 2003, and EPO 03027750.3, filed 02 Dec 2003. It is reiterated that applicant has not filed a certified copy of the EPO applications as required by 35 U.S.C. 119(b).

Objections Withdrawn

Applicant's Amendment, filed 8 Oct 2009, with respect to objections to claims 74, 76, 77, 79 and 80 over minor informalities has been fully considered and is persuasive, as amended claims 74, 76, 77, 79 and 80 recite scientific names properly italicized.

This objection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 8 Oct 2009, with respect to rejections of claims 68 and 69 under 35 USC 112, first paragraph, 35 U.S.C. 112, second paragraph; 35 U.S.C. 102(b); and 35 U.S.C. 103(a) has been fully considered and is persuasive, as claims 68 and 69 are canceled.

These rejections of claims 68 and 69 have been **withdrawn**.

The following are modified grounds of rejection necessitated by Applicant's Amendment, filed 8 Oct 2009, in which claims 49, 70 and 81 are amended to change the scope and breadth of the claim and claims 68 and 69 are canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 49-51 and 70-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 49-51 recite "a protected form thereof". Claims 70-82 depend from claims 49-51 and incorporate all limitations therein.

The specification discloses protected forms of KDG, such as wherein one or more of the hydroxyl groups at the positions 4, 5 and/or 6 are replaced by acetate ester or benzoate ester at page 5, paragraph 4 and page 6, paragraph 1 which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 49-51 and 68-82 are directed to encompass a protected form, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these protected forms meet the written description requirement of 35 USC 112, first paragraph, due to lacking chemical structural information for what they are and because chemical forms are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim. The protecting groups recited at page 5, paragraph 4 and page 6, paragraph 1 are provided as non-limiting examples.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 935 F.2d 1555, 1563 [19 USPQ2d 1111] (Fed. Cir. 1991), makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (*Vas-Cath* at page 1116.)

The recitation, "protected form", is seen to be merely functional language.

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added). There is no clear structural features commonly possessed by members of the genus of protected forms that distinguish it from other materials because there is no defined relationship between a specific chemical structure and the function of protecting a functional group. For example, exemplary protecting groups include an acetate ester, a silyl ether, a trityl ether or a benzylidine acetal.

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing

functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed protected forms, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. The court of *University of California v. Eli Lilly and Co.*, 119 F.3d 1559 [43 USPQ2d 1398] (Fed. Cir. 1997) held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

The court of *In re Curtis*, 354 F.3d 1347 [69 USPQ2d 1274] (Fed. Cir. 2004) held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when… the evidence indicates ordinary

artisans could not predict the operability … of any other species." The court of *Noelle v. Lederman,* 355 F.3d 1343 [69 USPQ2d 1508] (Fed. Cir. 2004) also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. The court of *Carnegie Mellon Univ. v. Hoffman-LaRoche Inc.*, 541 F.3d 1115, 1125 [88 USPQ2d 1233] (Fed. Cir. 2008) held that the written disclosure requirement was not met where the claims at issue covered a broad "genus of recombinant plasmids that contain coding sequences for DNA polymerase ...from any bacterial source, [but] the narrow specifications of the[relevant patents] only disclose[d] the ... gene coding sequence from one bacterial source ...."

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description requirement of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that *Vas-Cath* makes clear that the written description requirement of 35 USC 112 is severable from its enablement provision. (See *Vas-Cath* at page 1115.)

Response to Applicant's Remarks:

Applicant's Remarks, filed 8 Oct 2009, have been fully considered and not found to be persuasive.

Applicant's note that the specification discloses the protected forms of KDG wherein one or more of the of the hydroxyl groups at positions 4, 5 and/or 6 are

replaced by a protecting group known in the art at the paragraph spanning page 5 and 6. However, the specification does not specifically define said "protected form" as recited in the claim to said form wherein one or more of the of the hydroxyl groups at positions 4, 5 and/or 6 are replaced by a protecting group. Therefore the genus of "protected form" is not limited to the form wherein the hydroxyl groups at positions 4, 5 and/or 6 are replaced by a hydroxyl group protecting group. While the function of a hydroxyl group protecting group reasonably conveys the structure of a genus to one of skill in the art, the function of a "protected form" of a molecule does not because of the myriad structures that can be used to protect a molecule.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-51 and 70-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 recites "A method for producing … 2'-deoxynucleoside precursors ..." Claims 50-51 and 70-82 depend from claim 49 and incorporate all limitations therein. The term "2'-deoxynucleoside precursors" renders the claims indefinite because one of skill in the art would not be readily apprised of the metes and bounds of the claimed method. For example, CO_2 may be made into 2-deoxyribose, a 2'-deoxynucleoside precursor, and it is unclear if the claimed method is to be interpreted as a method for producing CO_2. While the specification at paragraph 26 provides preferred examples of

2'-deoxynucleoside precursors, it does not provide a limiting definition that defines the metes and bounds of the claimed method.

Response to Applicant's Amendment and Remarks:

Applicant's Amendment, filed 8 Oct 2009, is persuasive with respect to claims 70-80, as amended claim 70 depends from pending claim 49 and finds sufficient antecedent basis; claims 79 and 80, as amended claim 79 depends from claim 78 and finds sufficient antecedent basis; and claim 81 and 82, amended claim 81 does not recite both a broad and narrow range.

Applicant's Remarks, filed 8 Oct 2009, have been fully considered and not found to be persuasive with regard to the cited "A method for producing … 2'-deoxynucleoside precursors ..." in claim 49.

Applicant notes that the specification at least at page 5, paragraph 2 (corresponding to paragraph 26 cited above) describes 2'-deoxynucleoside precursors. However, as recited above, the preferred examples are provided as a non-limiting definition and do not establish the metes and bounds of the claimed method. Page 5, paragraph 2 provides that the term "relates to compounds which can be easily converted into 2'-deoxynucleosides by applying methods known in the prior art". Applicant's remarks do not clarify whether the claimed method is to be interpreted as encompassing a method for producing CO_2 and do not address the non-limiting nature of the examples in the specification as cited. Therefore this rejection is maintained.

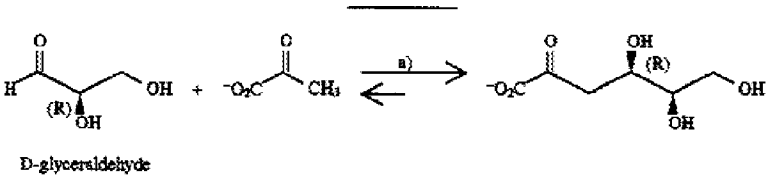
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

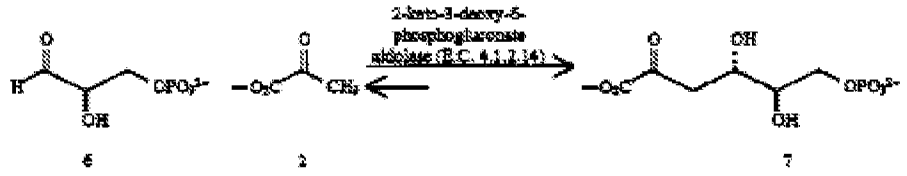
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United lStates.

Claims 49-51, 68-74, 78 and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong (US Patent 5,759,825, issued 02 Jun 1998, cited in PTO-892).

Wong discloses method comprising adding pyruvate decarboxylase to a 2-ketoaldonic acid (column 1, lines 20-25 and column 2, lines 20-35). Wong discloses the method wherein the 2-ketoaldonic acid made is a 2-keto-3-deoxy aldonic acid



(Scheme II(e) at bottom of columns 7 and 8). Wong envisions the method wherein the 2-ketoaldonic acid is made by an aldolase that reacts by si face attack at the carbonyl to give the (S) enantiomer at the C3 position such as sialic acid aldolase (column 16, lines 15-20), or such as



(example 18 spanning bottom of column29 and column 30, lines 10-50). Therefore one of skill in the art would instantly envision the method wherein the 2-ketoaldonic acid is made by reaction of D-glyceraldehyde and pyruvate using an aldolase that reacts by si face attack at the carbonyl to give the (S) enantiomer at the C3 position, or 2-keto-3-

deoxyglyconate, the compound of instant formula (I). Wong discloses the origin of the pyruvate decarboxylase (EC 4.1.1.1) may be selected from baker's yeast cells (column 3, lines 10-20), or *Saccharomyces cervisiae*, meeting limitations of instant claims 49-51, 70-74 and 78. Instant claim 78 recites further limitations of the benzoylformate decarboxylase but does not require the enzyme to be benzoylformate decarboxylase, therefore the method using pyruvate decarboxylase reads upon instant claim 78. Wong discloses the enzymatic reaction performed in a buffered solution at a pH from about 7.0 to about 7.5 (column 3, lines 60-65), meeting limitations of instant claim 81.

Wong is silent as to the decarboxylation reaction effected by pyruvate decarboxylase. However, it is apparent from what is disclosed that the decarboxylation reaction of the 2-ketoaldonic acid is necessarily present in the combination of reagents under the disclosed reaction conditions used to effect decomposition of pyruvate by the decarboxylation reaction of 2-ketoacid pyruvate catalyzed by pyruvate decarboxylase.

Response to Applicant's Remarks:

Applicant's Remarks, filed 8 Oct 2009, have been fully considered and not found to be persuasive.

Applicant notes that the enzyme pyruvate decarboxylase is added after denaturation of the previously added aldolase by acidification. Applicant reasons that under such acidic conditions the enzyme pyruvate decarboxylase would alter the specificity of said enzyme, therefore said enzyme may not necessarily implicitly effect a decarboxylation of the aldol disclosed by Wong. However, Wong at column 4, lines 20-35 provides that the mixture containing said aldol disclosed by Wong and excess

pyruvate to which said pyruvate decarboxylase is added has been adjusted to pH 6.5 following said acidic denaturation of aldolase and is maintained at pH 5.8 to 6.5. Wong discloses a similar result obtained with use of commercially available pyruvate decarboxylase instead of yeast (column 4, lines 65-70). Therefore it is reasonable to believe that the enzyme pyruvate decarboxylase in the mixture disclosed by Wong would inherently act upon said aldol disclosed by Wong according to the method of the instant invention.

Applicant notes that Wong teaches the decarboxylation of the aldol disclosed by Wong by non-enzymatic chemical reactions such as Barton's radical-mediated decarboxylation. Applicant notes that Wong does not teach the use of the enzyme pyruvate decarboxylase in order to effect a decarboxylation of the aldol. It is acknowledged that Wong discloses said pyruvate decarboxylase added in order to decompose excess pyruvate, and does not teach or fairly suggest the use of said pyruvate decarboxylase in order to effect a decarboxylation of the aldol disclosed by Wong. However, the same active step, adding said pyruvate decarboxylase to act upon the reaction mixture containing said aldol disclosed by Wong and excess pyruvate necessarily leads to same method performed. MPEP 2112.02 provides "Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device" citing *In re King,* 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986) and *Ex parte Novitski,* 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993).

Claim 49 recites the preamble “A method for producing producing 2’-deoxynucleosides or 2’-deoxynucleoside precursors from a compound of formula (I) or its salts or a protected form thereof in a process comprising a decarboxylation step;...” MPEP 2111.02 II. provides ‘The claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use "can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim."’ and citing *Metabolite Labs., Inc. v. Corp. of Am. Holdings*, 370 F.3d 1354, 1358-62, 71 USPQ2d 1081, 1084-87 (Fed. Cir. 2004), “The recitation of the intended use of "detecting" a vitamin deficiency in the preamble rendered the claimed invention a method for "detecting," and, thus, was not limited to detecting "elevated" levels. *Id.*” In view of the indefinite scope of the product produced by said method, the preamble is interpreted as an intended use or purpose of process, said process comprising said decarboxylation step.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 49-51, 68-78 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong (US Patent 5,759,825, issued 02 Jun 1998, cited in PTO-892) in view of Candy et al. (Biochimica et Biophysica Acta, 1998, 1385, p323-338, cited in PTO-892).

Wong discloses as above.

Wong does not specifically disclose the pyruvate decarboxylase is of prokaryotic origin (instant claim 75). Wong does not specifically disclose said prokaryotic organism is of the genus *Zymomonas*, *Zymobacter* or *Acetobacter* (instant claim 76). Wong does not specifically disclose said prokaryotic organism is of the species *Zymomonas mobilis, Zymobacter plamae* or *Acetobacter pasteurianus* (instant claim 77).

Candy et al. teaches pyruvate decarboxylase is known in the art as an equivalent enzyme known the same purpose of catalyzing the same reaction and teaches pyruvate decarboxylase or a corresponding DNA sequence has been found in *Saccharomyces cervisiae, Zymomonas mobilis* and species of *Acetobacter* (page 324, right column).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Wong in view of Candy et al. Candy et al. teaches that a pyruvate

decarboxylase from a different origin is known in the art as an equivalent enzyme. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious, see MPEP 2144.06 II.

Wong in view of Candy et al. is silent as to the decarboxylation reaction effected by pyruvate decarboxylase. However, it is apparent from what is disclosed that the decarboxylation reaction of the 2-ketoaldonic acid is necessarily present in the combination of reagents under the disclosed reaction conditions used to effect decomposition of pyruvate by the decarboxylation reaction of 2-ketoacid pyruvate catalyzed by pyruvate decarboxylase. While obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established, it is this invention *as a whole*, and not some part of it, which must be obvious under 35 U.S.C. 103, see MPEP 2141.02 V. The substitution of one known equivalent component for another is obvious, and the process made obvious by this substitution would inherently exhibit the decarboxylation reaction of the 2-ketoaldonic acid effected by pyruvate decarboxylase, therefore the invention *as a whole*, and not some part of it, is rendered obvious.

Response to Applicant's Remarks:

Applicant's Remarks, filed 8 Oct 2009, have been fully considered and not found to be persuasive.

Applicant's remarks with respect to Wong are addressed as above.

Applicant notes that with regard to the enzyme specificity of pyruvate decarboxylase, Candy et al. shows differences in reaction selectivity and kinetics

amoung different pyruvate decarboxylases. However, MPEP 2143.02 provides that "The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success." citing *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and *Ex parte Blanc*, 13 USPQ2d 1383 (Bd. Pat. App. & Inter. 1989), and that "Obviousness does not require absolute predictability, however, at least some degree of predictability is required." Wong discloses a similar result obtained with use of commercially available pyruvate decarboxylase instead of yeast (column 4, lines 65-70). Therefore within the context of the invention of Wong there is a reasonable expectation of success in combining Wong in view of Candy et al. With regard to the Wong in view of Candy et al. inherently rendering obvious the instant invention, MPEP 716.07 provides "Where the affidavit or declaration presented asserts that the reference relied upon is inoperative, the claims represented by applicant must distinguish from the alleged inoperative reference disclosure." The invention inherently rendered obvious by Wong in view of Candy et al. appears to be encompassed within the instant invention as claimed, and therefore is presumed operable by one skilled in the art.

Claims 49-51, 68-74, 81 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong (US Patent 5,759,825, issued 02 Jun 1998, cited in PTO-892). The CRC Handbook of Chemistry and Physics (Handbook of Chemistry & Physics Online, accessed online at www.hbcpnetbase.com, cited in PTO-892) provides evidence of the level of skill in the art.

Wong discloses as above.

Wong does not specifically disclose the method wherein the acid is HCl, H_2SO_4, D-gluconic acid or 2-dehydro-3-deoxy-D-gluconic acid (instant claim 82).

The CRC Handbook of Chemistry and Physics, citing references from 1956 and 1955, provides evidence that the level of ordinary skill in the art is to use acids such as HCl to adjust the pH of a buffer solution.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Wong wherein the buffered solution at a pH from about 7.0 to about 7.5 (column 3, lines 60-65) is adjusted using an acid such as HCl. The CRC Handbook of Chemistry and Physics provides evidence that this routine optimization of buffers is well within the level of ordinary skill in the art, and that an acid such as HCl is well known to one of ordinary skill in the art for the adjustment of the pH of a buffer.

Wong is silent as to the decarboxylation reaction effected by pyruvate decarboxylase. However, it is apparent from what is disclosed that the decarboxylation reaction of the 2-ketoaldonic acid is necessarily present in the combination of reagents under the disclosed reaction conditions used to effect decomposition of pyruvate by the decarboxylation reaction of 2-ketoacid pyruvate catalyzed by pyruvate decarboxylase. While obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established, it is this invention *as a whole*, and not some part of it, which must be obvious under 35 U.S.C. 103, see MPEP 2141.02 V. The routine optimization of pH using an acid that is well known in the

art is obvious, and the process made obvious by this routine optimization would inherently exhibit the decarboxylation reaction of the 2-ketoaldonic acid effected by pyruvate decarboxylase, therefore the invention *as a whole*, and not some part of it, is rendered obvious.

Response to Applicant's Remarks:

Applicant's Remarks, filed 8 Oct 2009, have been fully considered and not found to be persuasive.

Applicant's remarks with respect to Wong are addressed as above.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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